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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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James B. Lorens

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EXAMINER

HADDAD, MAHER M

ART UNIT

PAPER NUMBER

1644

DATE MAILED: 06/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/935,124	Applicant(s) LORENS ET AL.	
	Examiner Maher M. Haddad	Art Unit 1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02 April 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,6,14-16,19,28 and 29 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,6,14,15,19,28 and 29 is/are rejected.
- 7) ☒ Claim(s) 16 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

Art Unit: 1644

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4/2/04 has been entered.

2. Claims 1, 6, 14-16, 19 and 28-29 are pending.

3. Claims 1, 6, 14-16, 19 and 28-29 are under examination as they read on a method for identifying a compound that modulates angiogenesis in vitro, wherein the compound is a small organic molecule.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1, 6, 14-15, 19 and 28-29 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for identifying a compound that modulates angiogenesis comprising contacting the compound with a cell expressing the ILKAP polypeptide of SEQ ID NO: 2 and determining the angiogenic or loss of angiogenesis phenotypic effect of the compound upon the cell expressing the ILKAP polypeptide, whereby the difference in the angiogenic or loss of angiogenesis effect as compared to the angiogenic or loss of angiogenesis effect in the absence of the compound indicates that the compound modulates angiogenesis. does not reasonably provide **enablement** for a method for identifying a compound that modulates angiogenesis comprising contacting the compound with a cell expressing an ILKAP polypeptide, wherein the ILKAP polypeptide "has at least 90% identity to an amino acid sequence of SEQ ID NO:2", and wherein the ILKAP polypeptide has an anti-angiogenic phenotype in claim 1, wherein the ILDAMP polypeptide "has at least 95% identity to an amino acid sequence of SEQ ID NO: 2" in claim 28. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with this claim.

The specification disclosure does not enable one skilled in the art to practice the invention without an undue amount of experimentation.

The specification discloses only a single amino acid sequence (SEQ ID NO:2) with a disclosed anti-angiogenic activity (e.g., page 45 at lines 7-9). The instant claims encompass in their breadth *any* polypeptide that "has at least 90% or 95% identity to amino acid sequence of SEQ ID NO:2".

Art Unit: 1644

However, Attwood (Science 2000; 290:471-473) teaches that “[i]t is presumptuous to make functional assignments merely on the basis of some degree of similarity between sequences. Similarly, Skolnick et al. (Trends in Biotech. 2000; 18(1):34-39) teach that the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate, in part because of the multifunctional nature of proteins (e.g., “Abstract” and “Sequence-based approaches to function prediction”, page 34). Even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the artisan’s best guess as to the function of the structurally related protein (see in particular “Abstract” and Box 2). Finally, even single amino acid differences can result in drastically altered functions between two proteins. For example, Metzler et al. (Nature Structural Biol. 1997; 4:527-531) show that any of a variety of single amino acid changes can alter or abolish the ability of CTLA4 to interact with its ligands CD80 and CD86 (e.g., summarized in Table 2). Thus it is unpredictable if any functional activity will be shared by two polypeptides having less than 100% identity over the full length of their sequences.

Reasonable correlation must exist between the scope of the claims and scope of the enablement set forth. In view on the quantity of experimentation necessary the limited working examples, the nature of the invention, the state of the prior art, the unpredictability of the art and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

Applicant’s arguments, filed 4/2/04, have been fully considered, but have not been found persuasive.

Applicant argues that the claimed methods now specify that the ILKAP polypeptide has at least 90% identity to a reference amino acid sequence. Methods for determining percent identity are disclosed in the specification and are also well known to those of skill in molecular biology. Applicant submits that these elements provide adequate guidance for routine identification of the nucleic [sic] acids of the invention. In addition, claims now specify that the compound is identified by examining its angiogenic or anti-angiogenic effect on a cell expressing ILKAP.

Applicant is relying upon certain biological activities and the disclosure of a single species to support an entire genus. The claims as written encompass a broad genus of polypeptides with an unlimited number of possibilities with regard to the length of the polypeptide sequence. Further, the enablement issues of making the protein still remain because the specification does not teach and provide sufficient guidance as to which amino acid of SEQ ID NO:2 would have been altered such that the resultant polypeptide would have retained the anti-angiogenic activity. In addition, variation up to 10% of SEQ ID NO: 2 (39X 19¹⁰) provide a range of activities, not all which are necessarily predictive of the anti-angiogenic activity. Therefore, absent the ability to predict which of these polypeptides would function as claimed, and given the lack of data on regions critical for activity, for one of skill in the art to practice the invention as claimed would require a level of experimentation that is excessive and undue.

Art Unit: 1644

Applicant submits that the rejection is based on the assertion of undue experimentation appears to be based on an assumption that enablement requires the description of each and every nucleic acid that could be used in the claimed methods. Applicant contends that such a requirement is not consistent with the patent laws. Applicant submits that using the conditions set forth in the claims and specification and routine methodology, any competent laboratory technician in a molecular biology laboratory could isolate and prepare appropriate constructs, transform cells, and identify those nucleic acids that encode an ILKAP protein of the invention having at least 90% identity to SEQ ID NO:2.

However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. Therefore, one skilled in the art at the time of the invention would not be able to predict which positions in the protein which are tolerant to change that will not result in abolishing the anti-angiogenic activity of the polypeptide. Consequently the skilled artisan would not know how to use the instant invention as broadly claimed. While experimental testing techniques using appropriate constructs and transform cells are available, it is not routine in the art to use such methods when the expectation of success is unpredictable based on the instant disclosure. Thus, it would require an undue amount of experimentation of one skilled in the art to practice the invention as broadly claimed.

6. Claim 16 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.


7. No claim is allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (571) 272-0845. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Art Unit: 1644

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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May 28, 2004


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